Results and conclusions of the European Intergroup EURO-LB02 trial in children and adolescents with lymphoblastic lymphoma

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Supplement 2: Further exclusion criteria

Further exclusion criteria were: participation in another clinical trial, pregnancy, lactation, human immunodeficiency virus infection or acquired immunodeficiency syndrome, severe immunodeficiency, previous organ transplantation, previous malignancy, pre-existing disease prohibiting chemotherapy as outlined in the protocol, previous chemotherapy or radiotherapy, and previous systemic corticosteroid treatment for more than 8 days within two months before the start of therapy according to the protocol in the EURO-LB02 trial.

Supplement 3: Minimal diagnostic requirements for tumor biopsies

Obligatory antibodies for all entities were TdT, CD3, CD79a, MPO and Ki67. CD34 was required in cases of TdT-negative results, and CD20 was required in cases negative for CD3 and CD79a.

The following panel was required for pB-LBL (ICD-O 9728/3): CD10 and μ-, κ-, and λ-expression.

The following antibody panel was required for T-LBL (ICD-O 9729/3): CD1a, CD4, CD8, and CD56. Optional antibodies for T-LBL (ICD-O 9729/3) were CD2, CD5, CD7, and βF1. Optional antibodies for CD56-positive T-LBL (ICD-O 9729/3) were perforin and granzyme B.

Supplement 4: Staging

Staging included chest computed tomography (CT) scans and abdominal ultrasound and/or magnetic resonance imaging (MRI) or CT. CNS disease was diagnosed in cases with ≥5 cells/μL in the CSF and morphologically identifiable blasts in cytospin preparations of CSF or in cases exhibiting cerebral/medullary infiltrates on cranial/spinal MRI and/or cranial nerve

palsy not caused by extradural lymphoma. BM involvement was diagnosed as ≥5% and <25% lymphoblasts in the BM aspiration smear. The St. Jude staging system was applied.[1]

In patients with a life-threatening mediastinal mass, the initiation of cytoreductive therapy and the withholding of invasive diagnostic procedures were recommended until the patients were stabilized. In patients undergoing delayed CSF or BM aspiration, the BM/CNS status was designated as unknown.

Supplement 5: Recommendations for infection prophylaxis and therapy

Prophylactic treatment of *Pneumocystis carinii* with trimethoprim-sulfamethoxazole was recommended for the entire therapy duration, including maintenance therapy. The administration of prophylactic treatments against further infections and for infection therapy was performed at the discretion of the participating groups.

Supplement 6: Detailed randomization procedures

Patients with T-LBL were first randomized using a factorial design to receive either prednisone (60 mg/m²/d) or dexamethasone (10 mg/m²/d) on days 8-28 during induction phase Ia, with dexamethasone representing the experimental arm (randomization 1), and second, to receive maintenance therapy until a total treatment duration of 24 months or 18 months was achieved, with 18 months designated as the experimental arm (randomization 2).

The groups included in both random assignments were balanced and stratified according to disease stage, study group, and, for the 2nd randomization, the use of corticosteroids in phase Ia. Randomizations 1 and 2 were performed within the first 7 days of the prednisone pre-phase and within 21 days after the beginning of maintenance therapy, respectively.

Supplement 7: Response criteria

Tumor responses were evaluated on day 33 of induction therapy. In cases with BM/CSF involvement at diagnosis, BM/CSF were re-evaluated on day 33. A non-response was defined

as less than 35% regression in tumor volume, persistence of >5% blasts in BM and/or the persistence of blasts in CSF on day 33. Non-responding patients were designated as treatment failures and were removed from the study. A relapse was defined as biopsy-proven re-growth or as disease recurrence in patients who had achieved a response on day 33 of induction therapy.

Supplement 8: Power and sample size calculations

For the first randomization, assuming a 3-year EFS of 80% with the reference treatment, 270 patients per arm were required to show an absolute difference of 10% in 3-year EFS from randomization, based on a 5% probability of type I error and 90% power using a bilateral formulation log-rank test (intent-to-treat analysis). For the second randomization, the probability of 3-year EFS after having survived event-free for 15 months after diagnosis was estimated to be 95%. Considering a non-inferiority range of 4% and a 5% probability of type I error, 450 patients were required in each arm to show equivalence at 80% power (primary analysis as treated). The recruitment for the second randomization was planned to be continued in a subsequent study.

Supplement 9: Monitoring of TDs

The absolute death rate observed in each treatment arm (and the whole study population) was planned to be compared to a reference rate to detect an absolute increase in the number of TDs according to a Wald sequential plan.

In the NHL-BFM 90 and 95 studies, 4 TDs were observed among 387 patients in therapy group I (Non-B-NHL), i.e., 1% (95% CI: 0.29-2.6%).

Based on this previous experience, we chose the following parameters: p_0=1% and p_1=4%, with α=5% and β=1%.

Using the Wald's test with these parameters, the boundaries were:

Number of patients with at least 30 weeks of follow up or TD	Number of TDs
3-41	3
42-87	4
88-133	5
134-179	6
180-225	7
226-271	8
272-300	9

Amended stopping rule after the 5th case of TD

Based on a compilation of TRM from previous trials by the CoALL, SFCE, PPLLSG and NOPHO study groups, 13 of 430 patients suffered from TRM in these trials (TRM rate 3%, 95% CI: 1.6-5.1%). We chose the following parameters based on this previous experience: p_0=2% and p_1=4%, with α=5% and β=1%.

Based on these assumptions, the risk of wrongly concluding that a substantial number of TDs occurred was equal to an α value of 5% (whereas the actual rate is equal to $p_0 \leq 2\%$).

Additionally, the power to detect an excess number of TDs was equal to a 1-β value of 99% (if the real rate was equal to p_1=4%).

Using Wald's test with these parameters, the boundaries were:

Number of patients with at least 30 weeks of follow-up* or TD	Number of TDs
6-28	5
29-62	6
63-97	7
98-132	8
133-166	9
167-201	10
202-235	11
236-270	12
271-305	13
306-339	14
340-374	15

*Thirty weeks approximates the period from the beginning of induction therapy until the beginning of maintenance therapy.

Supplement 10: Non-fatal severe adverse events (SAEs)

Reg. No.	Diagnosis	1st Randomization	Steroid admini-stered	Phase in which the SAE occurred	SAE

Reg. No.	Diagnosis	1st Randomization	Steroid admini-stered	Phase in which the SAE occurred	SAE
0016	T-LBL	Yes	Dex	Prot. M	Delayed elimination of MTX and impaired renal function
1027	T-LBL	Yes	Dex	Ia	Hepatopathy
1062	T-LBL	No	PRED	IIa	Psychosis after discontinuation of corticosteroids
1062	T-LBL	No	PRED	IIa	Sepsis (Hafnia alvei), ARDS
1064	pB-LBL	No	PRED	IIb	Bulbar syndrome, suspected MTX toxicity
1051	T-LBL	Yes	Dex	Ia	Sinus vein thrombosis
1105	T-LBL	Yes	Dex	Ia	Hypoproteinemia and hypokalemia
1109	T-LBL	Yes	Dex	Ia	Hepatotoxicity
1135	T-LBL	Yes	Dex	Ia	Addison crisis
1165	T-LBL	Yes	Dex	Prot. M	Fracture of the radius (traumatic)
1165	T-LBL	Yes	Dex	IIa	Enteritis
1165	T-LBL	Yes	Dex	IIb	Suspected appendicitis and appendectomy
2004	T-LBL	Yes	Dex	Ia	Hemorrhagic varicella infection
4004	T-LBL	Yes	Dex	Ib	Septicemia (*S. aureus*)
4015	T-LBL	No data	Dex	Ia	*Pneumocystis carinii* infection
5021	T-LBL	Yes	Dex	Ia	Convulsions, coma, fever, and paresis
6048	T-LBL	Yes	Dex	Ia	Thrombosis of the femoral vein
6048	T-LBL	Yes	Dex	IIa	Allergic reaction to asparaginase
6053	T-LBL	Yes	Dex	Ia	Dysphagia and laryngeal palsy

Reg. No.	Diagnosis	1st Randomization	Steroid admini-stered	Phase in which the SAE occurred	SAE
6067	T-LBL	Yes	Dex	Ia	Hypovolemic shock and grade 4 diarrhea
6067	T-LBL	Yes	Dex	Ia	Cerebral thrombophlebitis
6074	T-LBL	Yes	Dex	maintenance	Vomiting and paresthesia
6074	T-LBL	Yes	Dex	maintenance	Osteonecrosis
6075	T-LBL	Yes	Dex	Ia	Enterocolitis
6075	T-LBL	Yes	Dex	Ia	Pulmonary bilateral invasive aspergillosis
8001	T-LBL	Yes	Dex	Ia	Severe colitis
8003	T-LBL	No	Dex	Ia	Thrombosis of the right femoral vein
1009	T-LBL	Yes	Pred	Ia	Necrotizing pancreatitis
1009	T-LBL	Yes	Pred	Ia	Cerebral seizures resulting from hypertensive encephalopathy due to renal insufficiency
1012	T-LBL	Yes	Pred	Ia	Hepatotoxicity and pancreatitis
1033	T-LBL	Yes	Pred	Prot. M	Hemiparesis
1065	pB-LBL	No	Pred	Prot. M	Neurological abnormalities after MTX treatment
1078	pB-LBL	No	Pred	Prot. M	Impaired MTX excretion
1084	pB-LBL	No	Pred	Prot. M	Impaired MTX excretion
1090	T-LBL	Yes	Pred	Ia	Sinus vein thrombosis
1119	T-LBL	No	Pred	Prot. M	Anaphylactic shock after MTX treatment
1127	pB-LBL	No	Pred	Ia	Severe pancreatitis

Reg. No.	Diagnosis	1st Randomization	Steroid admini-stered	Phase in which the SAE occurred	SAE
1128	Bi-LBL	Yes	Pred	Prot. M	Severe neurological abnormalities after high dose MTX treatment
1128	Bi-LBL	Yes	Pred	IIa	Attempted suicide (grade 4 depression)
1129	T-LBL	Yes	Pred	Ia	Toxic encephalopathy with loss of consciousness and respiratory insufficiency
1136	T-LBL	Yes	Pred	IIa	Need for ventilation and seizures with unconsciousness
1142	T-LBL	Yes	Pred	IIa	Pulmonary aspergillosis
1144	pB-LBL	No	Pred	IIa	Increased intraocular pressure
1150	pB-LBL	No	Pred	Prot. M	CNS bleeding in the right temporal lobe
1169	pB-LBL	No	Pred	IIa	Colon perforation
1174	pB-LBL	No	Pred	Ia	Severe hypoproteinemia, sepsis and infection with *C. difficile*
1182	pB-LBL	No	Pred	Ia	Intradural bleeding after therapeutic lumbar puncture
1807	T-LBL	No	Pred	IIa	Sepsis induced by *Pseudomonas aeruginosa*
2007	pB-LBL	No	Pred	Ia	Duodenal perforation

Reg. No.	Diagnosis	1st Randomization	Steroid admini-stered	Phase in which the SAE occurred	SAE
2016	T-NHL nfc	Yes	Pred	IIa	*E. coli*-induced sepsis, dexamethasone-induced diabetes mellitus, Herpes zoster infection (skin and eye)
2017	T-LBL	No	Pred	Ia	Seizures and PRES
2018	T-LBL	No	Pred	Ia	Varicella zoster infection and disseminated candida infection
2021	pB-LBL	No	Pred	Ib	Arterial hypotension requiring catecholamine therapy
2021	pB-LBL	No	Pred	IIa	Diabetes mellitus
2021	pB-LBL	No	Pred	IIb	Seizures
5032	T-LBL	Yes	Pred	IIa	Polyneuropathy
6028	T-LBL	No	Pred	Ia	Pneumopathy (CMV)
6028	T-LBL	No	Pred	IIa	Generalized seizures
6057	T-LBL	No	Pred	IIb	Diffuse interstitial pneumonia
6057	T-LBL	No	PRED	I/a	Left leg phlebitis
6059	pB-LBL	No	Pred	IIa	Septic shock
6062	Bi-LBL	No	Pred	Ib	Hemorrhagic cystitis (BK virus)
6062	Bi-LBL	No	Pred	IIa	Alveolitis grade 3
6065	T-LBL	Yes	Pred	maintenance	Osteonecrosis
6080	pB-LBL	No	Pred	Prot. M	Partial convulsions

Supplement 11: Grade III and IV toxic AEs observed during the pre-phase and in induction phase Ia.

Phase	Pre-phase			Ia - Prednisone			Ia - Dexamethasone			
Toxicity grade		III	IV		III	IV		III	IV	
	N	%	%	N	%	%	N	%	%	p†
Hemoglobin	305	2.6	.	208	13.9	1.9	102	26.5	7.8	**<0.001**
Leukocytes (total WBC)	306	1.6	0.3	210	16.2	8.6	101	19.8	27.7	**<0.001**
Granulocytes	279	1.8	1.1	190	17.9	13.2	93	15.1	34.4	**0.004**
Platelets	307	0.3	0.3	209	3.8	1.0	103	19.4	7.8	**<0.001**
PTT*	115	0.9	.	87	11.5	.	45	24.4	.	0.77
Fibrinogen*	112	1.8	.	87	32.2	12.6	41	34.1	9.8	1.00
Antithrombin*	106	.	.	83	22.9	2.4	41	31.7	4.9	0.212
Infection	309	1.9	0.3	210	6.2	0.5	103	12.6	3.9	0.009
Fever	306	.	0.3	208	1.0	.	101	2.0	2.0	0.092
Stomatitis	305	.	.	208	.	1.9	101	5.9	2.0	0.023
Diarrhea	307	.	.	209	1.4	1.4	104	1.9	5.8	0.078
Creatinine	306	0.3	.	206	0.5	.	101	.	1.0	0.55
Bilirubin	275	0.7	0.4	200	7.0	0.5	98	10.2	1.0	0.283
S-GOT/S-GPT	296	4.7	0.7	205	14.1	3.4	102	20.6	2.9	0.244
Cardiac function	275	1.1	0.7	163	.	0.6	89	2.2	1.1	0.128
Arrhythmia	296	0.7	0.3	189	.	.	97	3.1	1.0	0.013
Thrombosis/ embolism	305	3.3	.	207	7.7	.	99	16.2	.	0.029
Central neurotoxicity	308	0.3	.	209	0.5	4.3	103	2.9	3.9	0.441
Peripheral neurotoxicity	308	0.6	.	206	1.9	.	102	10.8	2.0	**<0.001**
Anaphylaxis	304	.	.	206	.	0.5	102	1.0	.	0.553
Osteonecrosis	288	.	.	193	.	.	95	1.1	.	0.330
Other scale	231	0.9	0.4	143	5.6	2.8	73	8.2	4.1	0.467

PTT, Partial thromboplastin time; N, number of patients with a valid report as to the individual criteria per treatment phase. *The number of patients in whom toxicity due to coagulation was documented is low since the documentation of coagulation began in March 2005.

†p-value for Fisher’s exact test of the difference in the frequency (grade III and IV combined) of patients receiving prednisone versus dexamethasone in induction phase Ia.

Supplement 12: Grade III and IV toxic AEs observed during protocols Ib, M, IIa and IIb.

Phase	Ib			M			IIa			IIb		
Toxicity grade		III	IV		III	IV		III	IV		III	IV
	N	%	%	N	%	%	N	%	%	N	%	%
Hemoglobin	303	48.5	37.6	291	16.2	3.8	251	23.5	3.2	244	48.0	13.9
Leukocytes (total WBC)	304	23.0	70.4	291	43.6	12.4	252	33.3	49.6	245	37.6	47.3
Granulocytes	282	14.5	79.8	266	32.7	27.4	231	17.7	67.5	225	28.0	60.4
Platelets	305	52.5	12.5	288	17.0	1.7	251	31.9	4.4	245	44.5	4.5
PTT*	109	7.3	.	95	7.4	.	102	12.7	.	68	11.8	.
Fibrinogen*	102	2.9	5.9	90	1.1	.	99	23.2	2.0	63	4.8	1.6
Antithrombin*	100	3.0	1.0	90	.	.	98	3.1	1.0	62	1.6	.
Infection	301	12.0	1.7	290	6.6	0.3	251	9.6	2.0	246	4.1	0.4
Fever	303	5.0	0.7	288	1.0	.	249	1.6	.	244	0.8	0.4
Stomatitis	302	3.0	0.3	292	5.8	2.4	252	7.9	4.8	246	.	.
Diarrhea	303	1.0	0.3	290	1.0	1.0	250	2.0	0.4	247	1.2	.
Creatinine	298	.	.	289	0.3	.	249	.	.	234	.	.
Bilirubin	286	5.6	0.3	272	2.2	.	237	1.3	.	221	.	.
S-GOT/S-GPT	293	22.2	2.4	285	10.5	1.4	246	11.0	2.4	231	12.6	0.4
Cardiac function	205	0.5	.	219	.	.	211	.	.	171	.	.
Arrhythmia	272	0.4	.	265	.	.	238	.	.	213	.	.
Thrombosis/ embolism	295	7.8	.	289	4.2	.	245	4.9	0.4	236	3.0	.
Central neurotoxicity	302	0.3	0.3	291	.	0.7	250	0.8	0.8	245	.	0.8
Peripheral neurotoxicity	300	1.0	.	292	0.3	.	249	2.0	.	244	.	0.4
Anaphylaxis	300	0.7	0.3	289	0.7	0.3	245	0.8	0.4	243	.	.
Osteonecrosis	277	0.4	.	267	.	0.4	226	0.4	0.4	224	.	.
Other scale	218	4.1	0.9	214	2.3	0.5	162	5.6	1.2	182	0.5	0.5

PTT, Partial thromboplastin time; S-GOT, serum glutamic-oxaloacetic transaminase; S-GPT, serum glutamic-pyruvic transaminase.

*The number of patients in whom toxicity due to coagulation was documented is low since the documentation of coagulation began in March 2005.

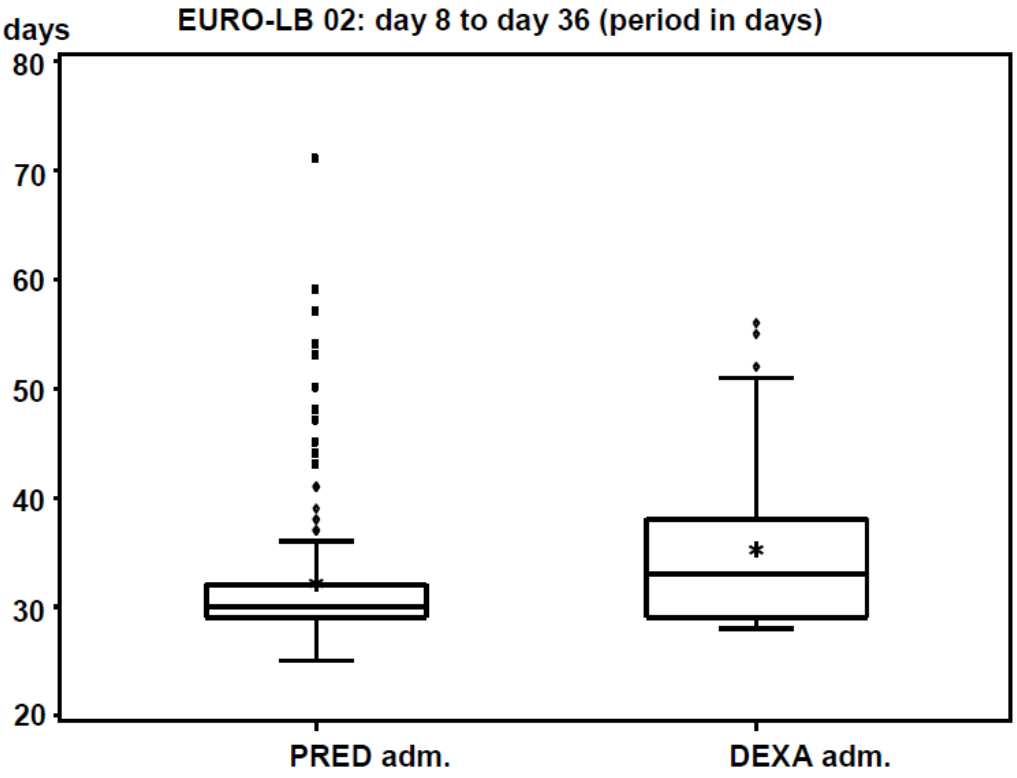
Supplement 13: Grade III and IV toxic AEs s in induction phase Ia – randomized patients only.

			AE grade (score)*						p†
		N	Toxicity grade 0-II		Toxicity grade III		Toxicity grade IV		
			N	%	N	%	N	%	
Hemoglobin	**Ia Prednisone**	89	77	86.5	10	11.2	2	2.2	**0.001**
	Ia Dexamethasone	95	62	65.3	26	27.4	7	7.4	
Leukocytes	**Ia Prednisone**	89	62	69.7	16	18.0	11	12.4	**0.034**
	Ia Dexamethasone	94	51	54.3	19	20.2	24	25.5	
Granulocytes	**Ia Prednisone**	81	51	63.0	16	19.8	14	17.3	0.210
	Ia Dexamethasone	86	45	52.3	14	16.3	27	31.4	
Platelets	**Ia Prednisone**	88	84	95.5	3	3.4	1	1.1	**<0.001**
	Ia Dexamethasone	95	69	72.6	19	20.0	7	7.4	
PTT	**Ia Prednisone**	32	26	81.3	6	18.8	.	.	0.580
	Ia Dexamethasone	42	31	73.8	11	26.2	.	.	
Fibrinogen	**Ia Prednisone**	32	15	46.9	12	37.5	5	15.6	0.811
	Ia Dexamethasone	38	20	52.6	14	36.8	4	10.5	
Antithrombin	**Ia Prednisone**	31	19	61.3	11	35.5	1	3.2	1.000
	Ia Dexamethasone	38	24	63.2	12	31.6	2	5.3	
Infection	**Ia Prednisone**	89	83	93.3	6	6.7	.	.	**0.041**
	Ia Dexamethasone	95	79	83.2	13	13.7	3	3.2	
Fever	**Ia Prednisone**	87	87	100.0	.	.	.	.	0.247
	Ia Dexamethasone	94	91	96.8	2	2.1	1	1.1	
Stomatitis	**Ia Prednisone**	89	88	98.9	.	.	1	1.1	0.119
	Ia Dexamethasone	95	89	93.7	4	4.2	2	2.1	
Diarrhea	**Ia Prednisone**	89	86	96.6	1	1.1	2	2.2	0.334
	Ia Dexamethasone	96	89	92.7	1	1.0	6	6.3	
Creatinine	**Ia Prednisone**	86	86	100.0	.	.	.	.	1.000
	Ia Dexamethasone	93	92	98.9	.	.	1	1.1	
Bilirubin	**Ia Prednisone**	86	77	89.5	8	9.3	1	1.2	1.000
	Ia Dexamethasone	90	81	90.0	8	8.9	1	1.1	
S-GOT/S-GPT	**Ia Prednisone**	86	73	84.9	11	12.8	2	2.3	0.437
	Ia Dexamethasone	94	75	79.8	16	17.0	3	3.2	

		N	AE grade (score)*						p†
			Toxicity grade 0-II		Toxicity grade III		Toxicity grade IV		
			N	%	N	%	N	%	
Cardiac function	**Ia Prednisone**	72	72	100.0	.	.	.	.	0.249
	Ia Dexamethasone	83	80	96.4	2	2.4	1	1.2	
Arrhythmia	**Ia Prednisone**	82	82	100.0	.	.	.	.	0.122
	Ia Dexamethasone	89	85	95.5	3	3.4	1	1.1	
Thrombosis/ embolism	**Ia Prednisone**	87	79	90.8	8	9.2	.	.	0.258
	Ia Dexamethasone	91	77	84.6	14	15.4	.	.	
Central neurotoxicity	**Ia Prednisone**	89	86	96.6	.	.	3	3.4	0.333
	Ia Dexamethasone	95	88	92.6	3	3.2	4	4.2	
Peripheral neurotoxicity	**Ia Prednisone**	88	86	97.7	2	2.3	.	.	**0.010**
	Ia Dexamethasone	94	82	87.2	10	10.6	2	2.1	
Anaphylaxis	**Ia Prednisone**	87	86	98.9	.	.	1	1.1	1.000
	Ia Dexamethasone	94	93	98.9	1	1.1	.	.	
Osteonecrosis (avascular necrosis)	**Ia Prednisone**	81	81	100.0	.	.	.	.	1.000
	Ia Dexamethasone	88	87	98.9	1	1.1	.	.	
Other scale	**Ia Prednisone**	59	55	93.2	4	6.8	.	.	0.545
	Ia Dexamethasone	70	62	88.6	6	8.6	2	2.9	

N, number of patients with a valid report regarding the individual criteria per treatment phase; AE, adverse event; PTT, Partial thromboplastin time; S-GOT, serum glutamic-oxaloacetic transaminase; S-GPT, serum glutamic-pyruvic transaminase.
*according to the NCI-CTC
**The number of patients in whom toxicity due to coagulation was documented is low since the documentation of coagulation began in March 2005.
†p-value for Fisher's exact test of the difference in the frequency (grade III and IV combined) of patients receiving prednisone versus dexamethasone in induction phase Ia.

Supplement 14: Figure 3



Supplement 15. Univariate analyses of prognostic factors in patients with T-LBL only.

		n	EFS (%)	SE (%)	p	non-response/relapse (cumulative incidence)	SE (%)	p (gray)
Stage	I	0						
	II	8	75	15		25	16	
	III	150	81	3	0.56	13	3	0.43
	IV	49	88	5		12	4	
	unknown	26	81	8		19	8	
Stage IV	BM+/CNS-	37	86	6		14	6	
	BM-/CNS+	5	80	18	0.71	20	20	0.68
	BM+/CNS+	4	100	0		0	0	
LDH	≤2 UNL	128	80	4	0.35	15	3	0.35
	>2 UNL	103	84	4		12	3	
	≤4 UNL	206	82	3	0.80	14	2	0.79
	>4 UNL	25	84	7		12	7	
Mediastinal Tumor	no	17	76	10	0.58	12	8	0.73
	yes	216	82	3		14	2	
Pleural effusion	no	86	81	4	0.86	15	4	0.64
	yes	147	82	3		13	3	
Pericardial effusion	no	152	85	3	0.086	12	3	0.2
	yes	81	77	5		17	4	
Bone involvement	no	222	82	3	0.51	13	2	0.25
	yes	11	73	13		27	14	
B-symptoms (any)	no	162	83	3	0.54	12	3	0.26
	yes	71	80	5		17	5	
Performance status*	1	57	88	4		11	4	
	2	70	81	5	0.056	13	4	0.07
	3	40	87	5		13	5	
	4	31	84	7		6	4	
	5	34	65	8		29	8	
	1 to 4	198	85	3	0.0033	11	2	0.006
	5	34	65	8		29	8	
Initial complications, any	no	82	82	4	0.77	16	4	0.77
	yes	151	82	3		13	3	
Cell lysis syndrome	no	220	82	3	0.55	14	2	0.78
	yes	12	74	13		17	11	
Impaired renal function	no	224	82	3	0.68	14	2	0.24
	yes	8	88	12		0	0	
Mediastinal	no	105	82	4	0.95	14	3	0.90

tumor with respiratory impairment	Yes	127	82	3		13	3	
Vena cava syndrome	no yes	200 32	82 78	3 7	0.53	15 6	3 4	0.16
Age (years)	<10 ≥10	128 105	82 82	3 4	0.92	13 15	3 4	0.49
	<15 ≥15	211 22	82 76	3 10	0.68	13 24	2 10	0.27
Gender	male female	176 57	82 81	3 5	0.58	15 11	3 4	0.58
age >10	male female	80 25	82 80	4 8	0.46	16 12	4 7	0.98
age >15	male female	18 4	76 75	10 22	0.94	24 25	11 25	0.71
Corticosteroid administered in phase Ia	Pred Dex	136 97	79 85	3 4	0.16	17 9	3 3	0.06
Treatment delay day 8 – the beginning of phase Ib (days)	≤34 >34	157 60	84 88	3 4	0.36	13 10	3 4	0.48

*****Modified Karnofsky Index.

Supplement 16. Univariate analyses of prognostic factors in patients with pB-LBL only (presentation of selected variables only).

		n	EFS (%)	SE (%)	p	cumulative incidence of non-response/ relapse	SE (%)	p (gray) (%)
Stage	I	11	100	0	0.025	0	0	0.26
	II	18	89	7		6	6	
	III	20	55	11		25	10	
	IV	14	86	9		7	7	
	unknown	3	100	0		0	0	
Bone involvement	no	46	80	6	0.81	9	4	0.66
	yes	20	80	9		15	8	
B-symptoms (any)	no	60	82	5	0.46	8	4	0.10
	yes	6	67	19		33	21	
Performance	1	33	79	7	0.59	9	5	0.28
	2	24	83	8		13	7	
	3	7	86	13		0	0	
	4	2	50	35		50	50	
	5	0						
Age (years)	<10	44	75	7	0.097	14	5	0.19
	≥10	22	91	6		5	5	
	<15	61	79	5	0.26	12	4	0.40
	≥15	5	100	0		0	0	
Gender	male	40	81	6	0.80	13	5	0.38
	female	26	80	8		8	5	
age >10	male	13	92	7	0.82	8	8	0.41
	female	9	89	10		0	0	
age >15	male	3				0	0	
	female	2				0	0	
Corticosteroid administered in phase Ia	Pred	62	79	5	0.31	11	4	0.44
	Dex	4	100	0		0	0	
Treatment delay day 8 – the beginning of phase Ib (days)	≤34	53	83	5	0.65	10	4	0.78
	>34	12	75	13		8	8	

Legends

Figure 3. Interval from day 8 of induction phase Ia until day 36 (beginning of induction phase Ib) according to the randomization arm.

References

1. Murphy SB. Classification, staging and end results of treatment of childhood non-Hodgkin's lymphomas: dissimilarities from lymphomas in adults. Semin Oncol. 1980;7:332-339.